combined end point of CHF-related death or hospital stay for CHF, mainly as the result of a reduced hospitalization rate. At baseline in both groups, a similar percentage of patients received angiotensin-converting enzyme inhibitors (ACEIs) and beta-blockers with a comparable percentage of recommended doses. At the end of the first 3 months, however, mean dosages of ACEIs and beta-blockers were significantly greater in the BNP group, which was considered to be the reason for the more favorable outcome of the BNP group.

These results are consistent with a previous smaller study suggesting superiority of N-terminal prohormone brain natriuretic peptide-guided treatment to clinically guided therapy (3). Although in that previous study beta-blockers were not yet generally prescribed, patients with CHF also received markedly lower dosages of ACEIs in the clinical group than in the BNP group.

However, in both studies, it does not appear conclusive why a patient who got blood drawn for BNP assessment should better tolerate up-titration of heart failure medication to target dosages. Thus, a considerable subset of patients in the clinical group "guided by guidelines" appears not to have been treated according to target dosages recommended in these guidelines.

Therefore, the study by Jourdain et al. (1) indicates that, for whatever reason, doctors are more likely to adhere to a target range of a surrogate parameter than to evidence-based recommendations of pharmacological doses and supports consequent up-titration to target doses in all CHF patients independent of BNP levels. To possibly support BNP-guided dosing, randomized trials are required assessing: 1) whether it is safe to keep patients on a low/moderate dose of ACEIs and beta-blockers after reaching normal BNP levels versus further up-titration to target dosages according to guidelines; and 2) whether patients with persistent elevated BNP levels despite target doses of ACEIs and beta-blockers benefit from dose increases beyond current target dosages if tolerated. In conclusion, currently available data do not yet justify a differential therapeutic strategy guided by BNP and do not support the superiority of BNP-guided treatment if doctors would more consequently adhere to dose recommendations of guidelines.

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Reply

We thank Dr. Hoppe for the interest in our report (1). The concern about the maximal treatment of the patients at baseline is of utmost importance. In the brain natriuretic peptide (BNP) group, mean angiotensin-converting enzyme inhibitor (ACEI) dosage increased from 96% of recommended dosage to 106% (i.e., some patients [36%] finally received dosage greater than that recommended by the European Society of Cardiology [ESC]). Similarly, the dosage of beta-blockade was increased as 58% of the patients received recommended dosage at baseline versus 77% after 3 months.

These figures are very high compared with those obtained in the large studies regarding beta-blockade: 43% (2) to 65% (3) received the target dose of beta-blockade in the COPERNICUS (Carvedilol Prospective Randomized Cumulative Survival Study Group), MERIT HF (Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure), CIBIS (Cardiac Insufficiency Bisoprolol Study)-II, or SENIORS (Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors with heart failure) trials. These figures are obtained in studies focused on beta-blockade, in which patient selection obviously limited the number of patients who were intolerant to beta-blockage. Besides, although most patients were receiving an ACEI or an angiotensin receptor blocker, the dosage of these drugs remains unpublished. Finally, triple therapy is infrequent in these studies, with a rate ranging from 20% to 28% of the patients when reported. In other words, optimal dosages have been determined in studies during which only one drug dosage was pushed to its maximum and, even so, tolerability was not perfect.

Accordingly, all registries report the use of lower dosages for all class of drugs. Even in recent randomized trials (including selected patients) evaluating nonpharmacological therapy, "optimal therapy" did not mean that all patients were receiving recommended dosages: for example, in CARE-HF (Cardiac Resynchronization Heart Failure Study) (4), 80% were receiving an ACEI, of whom 38% received more than 50% of recommended dosage. Similarly, 72% were receiving a beta-blocker, of whom 39% received more than one-half the recommended dosage. In conclusion, although it remains logical to recommend the target dose derived from randomized trial, it is not to be expected that all patients will tolerate all drugs at recommended dosages.

The last ESC guidelines on chronic heart failure including triple therapy were published in 2005 (5), after the STARS-BNP (Systolic Heart Failure Treatment Supported by BNP) study was completed (however, 33% of the patients included received a triple therapy at baseline). This triple therapy was recommended after the CHARM (Candesartan in Heart Failure) trial. Further illustrating our point, in this study, only 55% of the patients were receiving beta-blocker therapy (6), at an optimal dosage in an unknown proportion. Mean dosage of ACEI was 84% of that recommended by the ESC (vs. 96% in our study).

Therefore, there should not be confusion between recommendations for prescription, which is the aim, with expected prescription in the real life. Treatment at baseline was maximal in the STARS-BNP study. Logically, in the BNP group, "over-treatment" according to ESC guidelines was experienced in some patients after 3 months.

We agree with Dr. Hoppe that it would be interesting to know whether the dosage of the drugs for congestive heart failure could be decreased in a subset of patients, possibly identified using plasma BNP measurements, but this was not the aim of the STARS-BNP study. What the STARS-BNP study shows is that going beyond what is thought clinically by experts to be maximal treatment is beneficial in the group of patients with increased plasma BNP levels. We hope this simple message will allow improvement in patient management in the real world.

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